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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/590,375	06/09/2000	Keiji Endo	2173-0120P	2206

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EXAMINER

SLOBODYANSKY, ELIZABETH

ART UNIT	PAPER NUMBER
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1652

18

DATE MAILED: 02/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/590,375

Applicant(s)

ENDO ET AL.

Examiner

Elizabeth Slobodyansky

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 January 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) 7-9 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6, 10, 11 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

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## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 16, 2003 has been entered.

The AF amendment filed November 25, 2002 amending claims 1, 5 and 6 and adding claim 11 has been entered.

Claims 1-11 are pending. Claims 7-9 are withdrawn. Claims 1-6, 10 and 11 are under consideration.

### ***Drawings***

The formal drawings filed November 25, 2002 have been approved by Draftsman.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled

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in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim has been amended to encompass mutant  $\alpha$ -amylase comprising an amino acid sequence which is at least 70% homologous to SEQ ID NO:1. While there is support for a parent  $\alpha$ -amylase comprising an amino acid sequence which is at least 70% homologous to SEQ ID NO:1, the examiner is unable to locate adequate support in the specification for 70% homology for a mutant sequence. Thus, there is no indication that mutants having an amino acid sequence which is at least 70% homologous to SEQ ID NO:1 were within the scope of the invention as conceived by Applicants at the time the application was filed.

Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

Claims 1, 5 and 6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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Claim 1 is drawn to "a mutant  $\alpha$ -amylase obtained by making a substitution or deletion of at least one amino acid residue of specific positions in SEQ ID NO:1" or a sequence that is at least 70% homologous to SEQ ID NO:1, wherein said mutant  $\alpha$ -amylase possesses increased heat resistance and maintains resistance to chelating agents when compared to SEQ ID NO:1.

Claim 5 is drawn to a mutant  $\alpha$ -amylase obtained by introducing two kinds of mutations wherein a first/second mutation is a substitution or deletion of at least one amino acid residues in SEQ ID NO:1 or a sequence that is at least 70% homologous to SEQ ID NO:1, wherein said mutant  $\alpha$ -amylase possesses increased heat resistance and maintains resistance to chelating agents when compared to SEQ ID NO:1. Claim 6 depends on claim 5.

This rejection is made in view of the indefiniteness of the claims discussed below. The rejection is over mutants comprising mutations in addition to the mutations at the specified positions.

Therefore, the claims can be construed as drawn to mutants with unlimited number of mutations. In such case, the mutants may have any structure that is not necessarily homologous to SEQ ID NO:1.

Thus, the claims are drawn to an enormous genus of mutant  $\alpha$ -amylases characterized only by function.

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The specification discloses specific mutants of SEQ ID NO:1 mutated at the specific positions recited in the claims and specific combinations thereof. These mutations represent less than 1% of the structure of SEQ ID NO:1.

The specification fails to describe any other representative species by any identifying characteristics or properties other than the "functionality" of being a mutant  $\alpha$ -amylase with the requisite properties and fails to provide any structure: function correlation present in all members of the claimed genus.

Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 1-6, 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mutant  $\alpha$ -amylase obtained by a specific disclosed substitution at a single position selected from the group consisting of position 11, 16, 49, 84, 144, 167, 169, 178, 188, 190, 205 and 209 in SEQ ID NO:1, specific multiple mutants mutated at positions 167/169, 190/209, 144/190/209, 16/144/190/209, 167/169/190/209, 107/167/169/190/209, 49/107/167/169/190/209, 49/107/205/167/169/190/209 of SEQ ID NO:1 and a hybrid  $\alpha$ -amylase comprising residues 1-21 of SEQ ID NO:2 linked to residues 20-480 of SEQ ID NO:1 and said

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hybrid comprising specific mutations 167/169/190/209, wherein said mutants have increased heat resistance and maintain resistance to chelating agents when compared to SEQ ID NO:1, does not reasonably provide enablement for a mutant of an  $\alpha$ -amylase having at least 70% homology thereto with said mutations, wherein said  $\alpha$ -amylase mutants either have increased heat resistance and maintain resistance to chelating agents when compared to SEQ ID NO:1 or have unspecified properties. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 1-6 and 10 are so broad as to encompass any mutant of  $\alpha$ -amylase having at least 70% homology to SEQ ID NO:1 in which the amino acid corresponding to the specific positions in SEQ ID NO: 1 are mutated, said mutant  $\alpha$ -amylase having increased heat resistance and maintain resistance to chelating agents. Claim 11 encompasses any mutant of an  $\alpha$ -amylase having at least 70% homology to SEQ ID NO:1 in which the amino acid corresponding to the specific positions in SEQ ID NO: 1 are mutated, said mutant  $\alpha$ -amylase having unspecified properties. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of mutant  $\alpha$ -amylases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's

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amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the mutants of a single  $\alpha$ -amylase having the amino acid sequence of SEQ ID NO:1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass mutants of any  $\alpha$ -amylase with at least 70% homology to SEQ ID NO:1 in which the amino acid corresponding to specific residues recited in the claims are mutated because the specification does not establish: (A) regions of the protein structure which may be modified without effecting  $\alpha$ -amylase activity; (B) the general tolerance of amylases to modification and extent of such tolerance; (C) a rational and

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predictable scheme for modifying any  $\alpha$ -amylase residues with an expectation of obtaining any desired  $\alpha$ -amylase activity or  $\alpha$ -amylase activity combined with increased heat resistance and resistance to chelating agents; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make the claimed invention in a manner reasonably correlated with the scope of the claims broadly including amino acid modifications of any  $\alpha$ -amylase with at least 70% homology to SEQ ID NO:1 in which the amino acid corresponding to the specific residues in SEQ ID NO:1 are mutated. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of mutant  $\alpha$ -amylases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 1-6 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, with dependent claim 10, is unclear as reciting "at least one amino acid residue". It is unclear whether the scope of the claim is limited to sequences that differ from SEQ ID NO:1 by mutations consisting of at least one of the specific positions recited in the claim or includes sequences that have additional mutations.

Claims 2-4 recite "liquefying  $\alpha$ -amylase". The specification defines this term by non-limiting examples (pages 5-6).

Claims 2 and 5 are unclear as reciting "a substitution of a sequence ... from the amino terminus of SEQ ID NO:1" (emphasis added). It is unclear from which residue the amino terminus starts.

Claim 5 recites "a first [second] mutation is ..." (emphasis added). It is unclear whether "is" intended to be a closed or open language.

Claim 6 is confusing because it recites "first/second mutation comprises" whereas claim 5 from which claim 6 depends recites "first/second mutation consisting of" (emphasis added).

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***Response to Arguments***

Applicant's arguments filed November 25, 2002 have been fully considered but they are not persuasive.

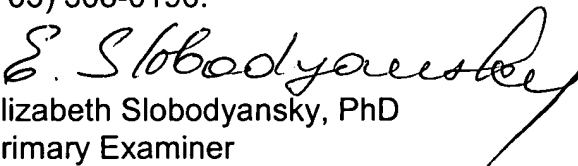
Applicants argue that "claim 1 is amended to clarify that the resulting mutant  $\alpha$ -amylase is at least 70% homologous to SEQ ID NO:1. As such, the instant claims do not encompass sequences having less than 70% homology to SEQ ID NO:1. For this reason, the rejection is overcome" (Remarks, page 8). This is not agreed with for the reasons stated above in the enablement rejection.

There are no further arguments related to the current rejections of the amended claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

  
Elizabeth Slobodyansky, PhD  
Primary Examiner

February 21, 2003